INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/019229

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/11 A61K31/7088 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 6 518 417 B1 (SCZAKIEL GEORG AND PATZEL VOLKER) 11 February 2003 (2003-02-11) the whole document column 2, lines 15-22; sequences 4-121 column 4, lines 51-56 -----	21,24, 25,27, 30,31 1-4, 13-15,20
Y	HOLEN T ET AL: "Similar behaviour of single-strand and double-strand siRNAs suggests they act through a common RNAi pathway" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 31, no. 9, 1 May 2003 (2003-05-01), pages 2401-2407, XP002281439 ISSN: 0305-1048 the whole document -----	1-4, 13-15,20
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 December 2004	16. 09. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Macchia, G

Form PCT/ISA/210 (second sheet) (January 2004)

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International Application No
PCT/US2004/019229

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	GILADI H. ET AL.: "Small interfering RNA inhibits hepatitis B virus replication in mice" MOLECULAR THERAPY, vol. 8, no. 5, November 2003 (2003-11), pages 769-776, XP008040415 siRNA-1 the whole document	1,2,13, 21
P,X	WO 03/070918 A (RIBOZYME PHARMA INC (US) MCSWIGGEN BEIGELMAN MACEJAK ZINNEN PAVCO ET A) 28 August 2003 (2003-08-28) page 75, lines 15-21 SEQ ID NO:425, 426: RPI#30350/30361 page 146 page 116 - page 118; figures 24,25; example 13	1-4, 13-15, 20,21, 24,30,31
A	MCCAFFREY A.P. ET AL.: "Inhibition of hepatitis B virus in mice by RNA interference" NATURE BIOTECHNOLOGY, vol. 21, no. 6, 1 June 2003 (2003-06-01), pages 639-644, XP008040439 HBVU6no.1 the whole document	
A	ANDINO R.: "RNAi puts a lid on virus replication" NATURE BIOTECHNOLOGY, vol. 21, no. 6, 1 June 2003 (2003-06-01), pages 629-630, XP002311173 the whole document	
A	SHLOMAI A. AND SHAUL Y.: "Inhibition of hepatitis B virus expression and replication by RNA interference" HEPATOLOGY, vol. 37, no. 4, April 2003 (2003-04), pages 764-770, XP008040408 the whole document	
A	COUZIN J.: "Mini RNA molecules shield mouse liver from hepatitis" SCIENCE, vol. 299, 14 February 2003 (2003-02-14), page 995, XP002310940 the whole document	

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/019229

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HAMASAKI K. ET AL.: "Short interfering RNA-directed inhibition of hepatitis B virus replication" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 543, no. 1-3, 22 May 2003 (2003-05-22), pages 51-54, XP004425032 ISSN: 0014-5793 the whole document	
A	WILSON J.A. ET AL.: "RNA interference blocks gene expression and RNA synthesis from hepatitis C replicons propagated in human liver cells" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 100, no. 5, 4 March 2003 (2003-03-04), pages 2783-2788, XP002300963 ISSN: 0027-8424 the whole document	
A	MCCAFFREY A.P. ET AL.: "RNA interference in adult mice" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 418, no. 6893, 4 July 2002 (2002-07-04), pages 38-39, XP002234152 ISSN: 0028-0836 the whole document	
A	KAPADIA S.B. ET AL.: "Interference of hepatitis C virus RNA replication by short interfering RNAs" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 100, no. 4, 18 February 2003 (2003-02-18), pages 2014-2018, XP002251050 ISSN: 0027-8424 the whole document	
A	SEO MI YOUNG ET AL.: "Small interfering RNA-mediated inhibition of hepatitis C virus replication in the human hepatoma cell line Huh-7" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 77, no. 1, January 2003 (2003-01), pages 810-812, XP002261781 ISSN: 0022-538X the whole document	

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-14 and 9-13 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-4, 9-15, 18-21, 23-27, 30, 31 all partially

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:1.
Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.
A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:25 or SEQ ID NO:26.

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2. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:2.
Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.
A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:23 or SEQ ID NO:24.

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3. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:3.
Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.
A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22.

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4. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:4.
Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.
A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:16 or SEQ ID NO:17.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

5. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8.
Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.
A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:14 or SEQ ID NO:15.

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6. claims: 1-4, 9-15, 18-21, 23-25, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:9.
Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.

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7. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:10.
Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.
A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:18.

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8. claims: 5-13, 16-20, 22-25, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis C virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:11.
Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.

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9. claims: 5-13, 16-20, 22-25, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:12.
Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. claims: 28-31 all partially

A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:27.
Expression construct and mammalian cell related thereto.
A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43 or SEQ ID NO:44.

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11. claim: 28 partially

A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:28.

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6518417 B1	11-02-2003	DE 19725803 C1	11-02-1999
		WO 9858055 A2	23-12-1998
		EP 0986642 A2	22-03-2000
WO 03070918 A	28-08-2003	NONE	